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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,015	12/02/2003	Andrew Geall	1530.0610001/EKS/J-H	3181

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/725,015	GEALL ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23-27* is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/8/07 has been entered.

Claims 1-27 are pending and under consideration in this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 10-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al (WO 02/00844) in view of Hunter et al (US Patent 5,811,088).

Evans taught methods of formulating DNA vaccines by mixing a cationic surfactant such as benzalkonium chloride (BAK), a polyoxypropylene (POP)-polyoxyethylene (POE) copolymer such as CRL 1005, and a polynucleotide at a temperature below the cloud point of the copolymer (about 2-7°C). See paragraph

bridging pages 32 and 33. The concentration ranges of nucleic acid, copolymer, and cationic surfactant are preferably in the ranges of 0.5-7.5 mg/ml, 1-70 mg/ml, and 0.1-10 mM, respectively (see page 21, line 32 to page 22, line 8. Evans stated that "[t]he inclusion of the cationic surfactant results in an increased percentage of polynucleotide that is physically associated with the block copolymer/cationic surfactant upon mixing and/or temperature cycling through the block copolymer cloud point, thus resulting in an enhanced in vivo immune response to polynucleotide vaccines and/or gene therapy-based transgenes." See page 3, lines 6-11. Thus Evans does not require "temperature cycling" through the cloud point. One of ordinary skill in the art at the time of the invention would appreciate that Evans performed temperature cycling in order to adjust the size of the particles formed by mixing the cationic surfactant, the POP-POE copolymer, and the polynucleotide. See page 33, lines 1-7. However, it is clear from the disclosure of Evans that the formation of the particle is what is desired, and that temperature cycling is not necessary to obtain it. As such it would have been obvious to one of ordinary skill in the art at the time of the invention to omit or include in the invention of Evans the step of temperature cycling depending on the desired size of the particles. In fact, Evans taught at page 34, Example 1 a method in which BAAK, CRL-1005 and DNA were mixed, frozen, and then thawed to a temperature above the cloud point. The diameter of the particles was then measured and found to be about 200 nm. The Example does not disclose the temperature at which the ingredients were initially mixed, but Evans disclosed at page 32 lines 23-26 that such mixtures were made at less than 5°C, so one of ordinary skill would have been motivated to mix the

components at that temperature, and could have obtained 200 nm particles without performing a complete temperature cycle (i.e. below cloud point, to above cloud point, to below cloud point).

Evans did not teach cold filtration of the formulation at any step in the process. However, it would have been obvious to one of ordinary skill in the art at the time of the invention that the formulations of Evans, intended for use as vaccines, should be sterile. Hunter taught that solutions comprising poloxamers can be sterilized by passage through a 0.22 micron filter at a cold temperature at which they are soluble. See column 18, lines 40-45. Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to cold filter formulations containing poloxamers at a temperature at which they are soluble, i.e. below their cloud point. As to the point in the method of Evans at which filtration would occur, it would clearly save time and materials to sterilize the nucleic acid, copolymer, and cationic surfactant after they had been mixed, rather than separately and individually prior to mixing. So filtration of the mixture is considered obvious to one of ordinary skill in the art at the time of the invention and could have been carried out at any time in the procedure. The mere rearrangement of steps would be *prima facie* obvious unless it can be shown that the rearrangement results in new or unexpected results (see MPEP 2144.04 (IV(C))). Thus the invention as a whole was prima facie obvious.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al (WO 02/00844), and Hunter et al (US Patent 5,811,088) as applied to claims 1-8 and 11-22 above, and further in view of Emanuele et al (US Patent 6,933,286).

The teachings of Evans and Hunter are set forth above and render obvious methods of formulating nucleic acids with POP-POE copolymers and cationic surfactants, and sterilizing the mixtures by cold filtration. In addition to the use of POE-POP-POE copolymers such as CRL 1005, Evans also taught the use of PLURONIC R copolymers, which have the general organization POP-POE-POP required by instant claim 9. See page 22, line 20 or Evans.

Evans did not teach a POP-POE-POP copolymer wherein POP accounted for up to 20 kDa of the mass of the copolymer, and POE represented between 1 and 50% of the copolymer by weight.

Emanuele taught formulations comprising POP-POE-POP copolymers and nucleic acids for delivery to animals. The POP portion accounted for up to 20 kDa of the mass of the copolymer and the POE portion represented from 1-90% of the copolymer by weight. In one embodiment POP was 2500 Da and POE was 10% of the copolymer mass. See the claims especially claims 1-5 and 8-12.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the copolymer of Emanuele in the method of Evans as modified by Hunter. One would have been motivated to do so because Evans suggested the use of POP-POE-POP copolymers, and Martin taught that when making nucleic acid/POP-POE-POP copolymer complexes for in vivo delivery one should use copolymers wherein POP

accounted for up to 20 kDa of the mass of the copolymer and POE represented from 1-90% of the copolymer by weight. Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 1/8/07 have been fully considered but they are not persuasive.

Applicant addresses the rejection at pages 7-10 of the response. The essence of the argument is that Evans does not teach a method in which the temperature of the mixture is not cycled above and below the cloud point of the poloxamer. This is unpersuasive for the reasons set forth in the rejection above. Specifically, Evans does not require temperature cycling (see page 3, lines 6-11). Evans seeks to form particles of nucleic acid, cationic surfactant, and copolymer, and indicates that this can be achieved by mixing these components at a temperature below the cloud point of the copolymer. Temperature cycling can then be used to adjust the size of the particles, but is not necessary. As a result, the step need not be included, and the claims are considered to be obvious.

Conclusion

Applicant's amendment overcame the rejection of claims 1-22 for new matter. Claims 23-27 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635